REMARKS

Reconsideration is requested.

Claims 67-85 are pending.

The specificaiton has been amended to include a cross-reference to the parent International Application, as may be required according to Rule 78.

Entry of the previously-filed Sequence Listing is acknowledged, with appreciation.

The claims have been amended above to obviate certain formal rejections to at least reduce some issues for appeal. Entry of the present Amendment is requested.

Claims 67 and 71 have been amended to obviate the objection to same stated in Section [10] of the Office Action dated May 16, 2006. Entry of the present Amendment and withdrawal of the objection are requested.

Claim 78 has been amended above as suggested by the Examiner in Section [11] of the Office Action dated May 16, 2006, to obviate the objection to claim 78. Entry of the present Amendment and withdrawal of the objection are requested.

The Section 112, second paragraph, rejection of claims 79 and 85 is believed to be obviated by the above amendments. Specifically, claim 79 has been revised above in response to the Examiner's comments contained in Section [12][a] of the Office Action dated May 16, 2006 to include a comparison. Moreover, claim 85 (and claim 84) have been revised above in response to the Examiner's suggestions in Section [12][b] of the Office Action dated May 16, 2006. Entry of the present Amendment and withdrawal of the Section 112, second paragraph, rejection of claims 79 and 85 are requested.

The Section 112, first paragraph "written description", rejection of claims 67-85 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

The description and claims define that the *Photinus pyralis* luciferase amino acid sequence of SEQ ID NO: 37 as the reference sequence against which the recombinant proteins can be compared. Claim 67, for example, defines a genus encompassing a recombinant protein which has luciferase activity, at least 90% similarity to the *Photinus pyralis* wild-type luciferase of SEQ ID NO: 37, a mutation corresponding to residue 214, of the *Photinus pyralis* luciferase, and increased thermostability compared to the *Photinus pyralis* wild-type luciferase. Representative examples within the scope of the claimed genus are described in the specification, including recombinant proteins with the following mutations compared to the wild-type *Photinus pyralis* luciferase (of SEQ ID NO: 37): T214A/I232A/E354K, T214A/I232A/E354K/A215L, I232A/E354K/T214A/F295L, I232A/E354K/T214A, I232A/E354K/T214A/F295L/F14A/L35A/A215L, T214A, T214C, and T214N, (see page 14, line 28 to page 15, line 9). Other representative examples of recombinant proteins of the invention are described in Examples 2-4 and 7.

The applicants submit that one of ordinary skill in the art would be aware of wild-type luciferases and that the applicants provide various distinguishing identifying characteristics of the claimed invention relating to structure (i.e. 90% similarity to the luciferase of SEQ ID NO: 37) and biological function (i.e. luciferase function and increased thermostability) of recombinant proteins relating to the *Photinus pyralis* wild-type luciferase. Thus, the ordinarily skilled person with his background knowledge when

reading the description and examples of the present application would appreciate that the applicants were in possession of the invention as claimed when the application was filed.

The applicants observe that, according to the USPTO "Revised Interim Written Description Guidelines Training Materials" available on the USPTO website, the "disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus" (page 31). The Examiner's attention is drawn in particular to Example 14 of the Training Materials, in which the exemplar claim is directed to a protein having a specific sequence and variants thereof with at least 95% identity to that sequence and capable of catalysing a specific biological reaction. The example provides that there is reduction to practice of the single disclosed species but that the claimed variants are contemplated but not exemplified. Yet the applicant is deemed to be in possession of the invention because the single species is representative of the claimed genus, all members of the genus must have a given structural identity to the given sequence, and there is an assay which would identify all of the claimed variants. By analogy with Example 14, the applicants submit that the present specification similarly provides an adequate written description, from which one of ordinary skill in the art would conclude that the applicants were in possession of the invention recited in the claims.

The applicants note that the term "similarity" is recited in the claims, which one of ordinary skill in the art will appreciate from the specification refers to a quantifiable parameter which involves measurement of sequence similarity between a recombinant protein and the wild-type luciferase of SEQ ID NO: 37 referred to in the claims. In the

present application at page 13, lines 9 - 24, it is stated that sequence similarity may in particular be assessed (i.e. quantified) using the well-known Lipman and Pearson (1985) multiple alignment method, and the exact parameters which should be used in determination of similarity are provided. An ordinarily skilled person comparing an "unknown" sequence with the reference sequence of SEQ ID NO: 37 would, using the Lipman and Pearson method referred to in the application, arrive at only one value of sequence similarity and be able to determine whether or not the unknown sequence fell with the scope of the claims.

The Section 112, first paragraph "enablement", rejection of claims 67-85 is traversed. Reconsidration and withdrawal of the rejection are requested in view of the following comments.

The applicants note that independent claim 67 covers recombinant proteins with luciferase activity, increased thermostability and at least 90% similarity compared to wild-type *Photinus pyralis* luciferase of SEQ ID NO: 37. As mentioned above, numerous representative examples within the scope of the claims are provided in the specification, and the applicants also provide clear teaching and guidance on how to make, test and use other species of recombinant proteins within the scope of the claims. The applicants submit that the amended claims are enabled for the reasons set out below.

The Examiner has referred to MPEP 2164.03 regarding predictability. However, in assessing enablement, MPEP 2164.01(a) also notes that the Examiner should consider several factors, including the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples,

and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. The Manual states that it is improper to conclude that a disclosure is not enabling based in an analysis of only one of the above factors while ignoring one or more of the others. The Examiner's analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole. This has been reinforced by the recent decision of Capon v. Eshhar v. Dudas (US Court of Appeals for the Federal Circuit, 12 August 2005), where the court stated that the determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter.

The applicants request that the Examiner takes into account all of the relevant factors regarding enablement and to not, for example, focus on only the aspect of predictability. Inventions in the biological sciences, for instance relating to recombinant proteins, may contain an amount of some unpredictability however if the same were an absolute bar to patentability, then it may not be possible for an applicant or patentee to claim a variant of a specific protein sequence by sequence identity or similarity variation. This would be contrary to the Patent Office practice, as evidenced by previously granted U.S. patent claims and the Training Materials of the USPTO (see for example, Example 14 of the USPTO "Revised Interim Written Description Guidelines Training Materials" mentioned above). With sufficient teaching in the specification on how to make and test variants, as has been provided in the present application, there is

no undue experimentation required by one of ordinary skill to make and use the full scope of the claimed invention. The applicants therefore respectfully submit that the application, as directed to one of ordinary skill and taking into account the state of the prior art, provides enablement for the claimed invention.

The Examiner is requested to hold the provisional obviousness-type double patenting rejection of claims 67-85 over claims 1-4, 6-10, 14, 17-19 and "6-23" of copending Application Serial No. 10/111,723 in abeyance until such time as allowable subject matter is identified.

Entry of the present Amendment, at least to place the application in better condition for appeal, is requested.

Respectfully submitted,

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